

In the claims:

1. (Currently Amended) A polypeptide that inhibits complement C1s, wherein the polypeptide is characterized by the formula: “P-N-[DE](2)-[YX₁X₂X₃]-[DE](1,2)-[YX₁X₂X₃]-[DE]-[YX₁X₂X₃]-[DE](1,2),” where amino acid residues in square brackets indicate ~~acceptable~~ alternative amino acids, numbers in parentheses indicate the number of amino acid residues, such that [DE](2) represents DD, EE, DE, or ED; “X₁” represents Phe-(*p*-CH₂)SO₃H, “X₂” represents sulfated tyrosine, and “X₃” represents 2-sulfotyrosine (SEQ ID NO:127).

2. (Original) The polypeptide of claim 1, wherein the polypeptide is characterized by the formula: “P-N-[DE](2)-[YX₁X₂X₃]-[DE](1,2)-[YX₁X₂X₃]-[DE]-[YX₁X₂X₃]-[DE]” (SEQ ID NO:129).

3. (Original) The polypeptide of claim 2, wherein the polypeptide is characterized by the formula: “P-N-E-E-[YX₁X₂X₃]-E-[YX₁X₂X₃]-E-[YX₁X₂X₃]-E” (SEQ ID NO:130).

4. (Original) The polypeptide of claim 3, wherein the polypeptide consists of the amino acid sequence: “PNEEY EYEYE” (SEQ ID NO:125).

5. (Currently Amended) A polypeptide that inhibits complement C1s, wherein the polypeptide comprises an amino acid sequence that is characterized by the formula: “[AP]-N-[DE](2)-[X₁X₂X₃]-[DE](1,2)-[X₁X₂X₃]-[DE]-[X₁X₂X₃]-[DE](1,2)” where amino acid residues in square brackets indicate ~~acceptable~~ alternative amino acids, numbers in parentheses indicate the number of amino acid residues, such that [DE](2) represents DD, EE, DE, or ED; “X₁” represents Phe-(*p*-CH₂)SO₃H, “X₂” represents sulfated tyrosine, and “X₃” represents 2-sulfotyrosine (SEQ ID NO:126).

6. (Original) A peptide or polypeptide that inhibits complement C1s, wherein the peptide or polypeptide comprises the amino acid sequence “CRLGC” (amino acid residues 64 to 68 of SEQ ID NO:1), wherein the peptide or polypeptide consists of five to thirty amino acid residues.

7. (Original) The peptide or polypeptide of claim 6, wherein the polypeptide consists of the amino acid sequence: "GCDGFKCRLG CTYGFKTDKK GCEAFCTCNT" (SEQ ID NO:53).

8. (Currently amended) The peptide of claim 6, wherein the peptide consists of the amino acid sequence: "CRLGC-" (amino acid residues 64 to 68 of SEQ ID NO:1).

9. (Cancelled) A complement C1s inhibitor, wherein the inhibitor consists of:

(a) a C1s catalytic site-directed moiety (CCSDM), which is selected from the group consisting of: (i) CH₃-Lys(Cbo)-Gly-Arg-pNA-AcOH, where "Cbo" represents benzyloxycarbonyl; (ii) CH₃-Lys(Cbo)-Gly-Arg; (iii) H-D-Val-Ser-Arg-pNA•HCl; (iv) H-D-Val-Ser-Arg; (v) Leu-Xaa-Arg, where "Xaa" represents alanine, glutamine, or glycine; (vi) LQRALEILPN RVTIKANRPF LVFI (SEQ ID NO:118), (vii) serine protease inhibitor; (viii) heterocyclic protease inhibitor; (ix) transition state analogue; (x) benzamidine; (xi) X-C1-C2-A-Y, where C1 is a derivative of Arg, Lys, or Orn, characterized by a reduced carboxylate moiety or a carboxylate moiety that is displaced from the α-carbon by a chemical structure characterized by a backbone chain of from 1 to 10 atoms, C2 is a non-cleavable bond, "X" is hydrogen or a continuation of the peptide backbone, "A" is a backbone chain, and "Y" is a bond; (xii) CDGFK CRLGC TYGFK TDKKG CEAFC TCNT (SEQ ID NO:121); and (xiii) X-C-X(8-12)-L-Q-R, where "X" represents glycine, serine, or threonine, and numbers in parentheses indicate the number of amino acid residues (SEQ ID NO:140);

(b) a linker moiety that is either characterized by a backbone chain having a calculated length of between 14 Å and 20 Å, or that is a polypeptide, which has the amino acid sequence of KETAC VNIWC TDPYK CNPES GRCD (SEQ ID NO:123); and

(c) a C1s exosite binding moiety (CEBM), which is selected from the group consisting of: (i) a polypeptide characterized by the formula: "[AP]-N-[DE](2)-[YX₁X₂X₃]-[DE](2)-[YX₁X₂X₃]-[DE]-[YX₁X₂X₃]-[DE](1,2)," where amino acid residues in square brackets indicate acceptable amino acids, numbers in parentheses indicate the number of amino acid residues, "X₁" represents Phe-(p-CH₂)SO₃H, "X₂" represents sulfated tyrosine, and "X₃" represents 2-sulfotyrosine (SEQ ID NO:126); and (ii) NEDYEDYEYD (SEQ ID NO:119);

wherein the C1s catalytic site-directed moiety is bound to the linker moiety, the linker moiety is bound to the C1s exosite binding moiety.

10. (Cancelled) The inhibitor of claim 9, wherein the serine protease inhibitor is selected from the group consisting of phenylmethanesulfonylfluoride, diisopropyl fluorophosphate, tosylpropylchloromethylketone, and tosyllysyl chloromethylketone.

11. (Cancelled) The inhibitor of claim 9, wherein the heterocyclic protease inhibitor is an isocoumarin.

12. (Cancelled) The inhibitor of claim 9, wherein the transition state analogue is difluoroketomethylene.

13. (Cancelled) The inhibitor of claim 9, wherein a moiety having the formula "X-C1-C2-A-Y" includes a C1 component selected from the group consisting of β -homoarginine, an arginine containing a reduced carboxylate moiety, and β -homomithine.

14. (Cancelled) The inhibitor of claim 13, wherein the arginine containing a reduced carboxylate moiety is Arg ψ [CH₂NH].

15. (Cancelled) The inhibitor of claim 13, wherein the linker is selected from the group consisting of: (i) A-L-[ED]-[ED]-X(1-3) (SEQ ID NO:131), (ii) A-L-X(1-3)-[ED]-[ED] (SEQ ID NO:132), (iii) A-L-[ED]-[ED] (SEQ ID NO:122), (iv) X(2-5)-[ED]-[ED] (SEQ ID NO:134), (v) A-L-[ED]-[ED]-X(1-2)-C (SEQ ID NO:136), (vi) A-L-[ED]-[ED]-C (SEQ ID NO:124), (vii) X(1-4)-[ED]-[ED]-C (SEQ ID NO:138), (viii) A-L-X(1-2)-[ED]-[ED]-C (SEQ ID NO:139), (ix) X(4-7) (SEQ ID NO:133), (x) X(5-7) (SEQ ID NO:135), and (xi) X(3-6)-C (SEQ ID NO:137), where amino acid residues in square brackets indicate acceptable amino acids, numbers in parentheses indicate the number of amino acid residues, and "X" represents any of glycine, serine, or threonine.

16. (Cancelled) A complement C1s inhibitor, wherein the inhibitor consists of:

(a) a C1s catalytic site-directed moiety (CCSDM), which is selected from the group consisting of: (i) GCDGFKCRLG CTYGFKTDKK GCEAFCTCNT (SEQ ID NO:53); and (ii) CRLGC (amino acid residues 64 to 68 of SEQ ID NO:1);

(b) a linker moiety characterized by a backbone chain having a calculated length of between 14 Å and 20 Å; and

(c) a C1s exosite binding moiety (CEBM), which is a polypeptide characterized by the formula: "A-N-[DE](2)-[YX₁X₂X₃]-[DE](2)-[YX₁X₂X₃]-[DE]-[YX₁X₂X₃]-[DE](1,2)," where amino acid residues in square brackets indicate acceptable amino acids, numbers in parentheses indicate the number of amino acid residues, "X₁" represents Phe-(p-CH₂)SO₃H, "X₂" represents sulfated tyrosine, "X₃" represents 2-sulfotyrosine (SEQ ID NO:128);

wherein the C1s catalytic site-directed moiety is bound to the linker moiety, the linker moiety is bound to the C1s exosite binding moiety.

17. (Cancelled) The complement C1s inhibitor of any one of claims 9 or 16, wherein the inhibitor is characterized by the formula: "CCSDM-Linker-CEBM."

18. (Original) A composition, comprising a carrier, and a peptide or a polypeptide of any one of claims 1, 5, or 6.

19. (Cancelled) A composition, comprising a carrier, and the complement C1s inhibitor of any one of claims 9 or 16.

20. (Cancelled) A method of inhibiting complement C1s inhibitor, comprising administering the composition of claim 18 to complement C1s.

21. (Cancelled) A method of inhibiting complement C1s inhibitor, comprising administering the composition of claim 19 to complement C1s.

22. (Cancelled) The method of claim 20, wherein the composition is administered to a mammalian subject.

23. (Cancelled) The method of claim 21, wherein the composition is administered to a mammalian subject.